

1, consistent with the recitation "n is 1 to 6" in claim 9, as amended. Thus, claims 17-19 are clear and definite.

Claims 9, 10, 20-22, 26 and 27 are alleged to be vague and indefinite for recitation of "about." The Office Action at page 3 appears to assert that Applicants must define the variable "n" in claim 9 as an integer and that "about 6" is not an integer. Although Applicants believe the claims are clear and definite as written, Applicants have amended the claims to delete the term "about" solely in order to advance prosecution of the present application.

The Office Action at page 3 asserts that claims 22 and 25 are substantial duplicates of one another. Applicants thank the Examiner for pointing out the typographical error in claim 25, and have amended claim 25 to depend from claim 10, as suggested by the Examiner. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claims 9, 15-22, 25¹ and 26 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent 5,013,830 (hereinafter, the "Ohtsuka reference"). Applicants respectfully request reconsideration of this rejection as the Ohtsuka reference fails to teach or suggest Applicants' claimed compounds.

With respect to claims 9 and 15-22, the Office Action suggests that the phrase "a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides" in claim 9 includes the 2'-O-methyl, -ethyl, and -propyl groups which are allegedly described by the Ohtsuka reference. This issue is

¹As suggested in the Office Action at page 3, Applicants have amended claim 25 to depend from claim 10. Since claim 10 is not included in the present rejection, the rejection will not be addressed with respect to amended claim 25.

believed to be moot, however, as Applicants have amended claim 9 to delete the recited phrase. In view of this, Applicants request that the rejection of claims 9 and 15-22 be withdrawn.

With respect to claim 26, the Office Action appears to assert that it would have been obvious to one of ordinary skill in the art to substitute a methyl, ethyl or propyl moiety at the 2'-O position of guanosine since the Ohtsuka reference allegedly teaches modifying nucleosides in such a manner in general. This issue is believed to be moot, however, as Applicants have amended claim 26 to recite "C₄-C₂₀ alkyl," support for which can be found at, for example page 12, lines 7-9 of the specification. In view of this, Applicants request that the rejection of claim 26 be withdrawn.

Claims 10, 23, 24 and 27 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Ohtsuka reference in view of Kikuchi, et al., Chem. Abstract No. 110:24228w (hereinafter, the "Kikuchi reference"). Applicants respectfully request reconsideration of this rejection as the suggested combination of references would not produce any claimed compound.

As best understood, what the Office Action suggests is that the only difference between the pending claims and the compounds of the Ohtsuka reference is the presence of a 2-aminoadenosine base. The Office Action further asserts that it would have been obvious to one of ordinary skill in the art to replace the adenosine nucleosides of the Ohtsuka reference with 2-aminoadenosine nucleosides since the Kikuchi reference teaches that adenosine can be replaced by 2-aminoadenosine. However, the Office Action fails to provide any motivation to combine the teachings of the cited references. The Kikuchi reference merely describes oligonucleotides which include 2-aminoadenosine. In any event, the apparent basis for this rejection is that the phrase "a group that enhances the pharmacodynamic properties of

oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides" allegedly includes 2'-O-methyl, -ethyl, and -propyl groups disclosed by the Otsuka reference. Since, as noted above, this issue is rendered moot by deletion of the indicated phrase from claim 10, Applicants request that the rejection of claims 10, 23, 24 and 27 be reconsidered and withdrawn.

Claim 24 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Otsuka reference in view of the Kikuchi reference and Iribarren, et al. (*Proc. Natl. Acad. Sci. USA, 1990, 87, 7747*, hereinafter, the "Iribarren reference.") Applicants respectfully request reconsideration of this rejection as the suggested combination of references would not produce any claimed compound.

The Office Action asserts at page 5 that the only deficiency in the Otsuka and Kikuchi references is the lack of a 2'-O-allyl derivative, and that it would have been obvious to one of ordinary skill in the art to add a 2'-O-allyl group from the Iribarren reference to the compounds that allegedly would have been produced by combining the teachings of the Otsuka and Kikuchi references. Even if the references are combined in such a manner, none of Applicants' claimed compounds are produced. The compounds of claim 24 comprise a substituted C₄-C₂₀ alkenyl group. There is no teaching or suggestion in any of the cited references to further modify any compounds to produce Applicants' claimed compounds. Accordingly, Applicants respectfully request that the rejection of claim 24 be withdrawn.

In view of the amendments to the claims and the foregoing comments, Applicants respectfully request that the rejections under 35 U.S.C. §103(a) be withdrawn.

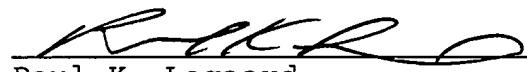
Applicants submit that the claims patentably define the invention over the applied art and are otherwise in condition for

ISIS-0710

PATENT

ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,



Paul K. Legaard
Registration No. 38,534

Date: November 21, 1997

WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100